TNF-α −857 and −308 ($\chi^2 = 23.88$, $P < 0.001$) or −238 ($\chi^2 = 13.91$, $P < 0.005$) and between *TNF-α* −376 and −238 ($\chi^2 = 363.47$, $P < 0.001$). *TNF-α* −857 T/T genotype was more frequent in patients with duodenal ulcer than in those with noncardia gastric cancer or other benign diseases, considering the patients overall ($\chi^2 = 38.78$, $P < 0.01$) or only those *H. pylori* infected ($\chi^2 = 34.65$, $P < 0.05$) or infected by *cagA* positive strains ($\chi^2 = 12.50$, $P < 0.05$) (Figure 1). The risk of duodenal ulcer for the *TNF-α* −857 T/T genotype was 4.28 (95% CI, 1.80–10.21). *TNF-α* −857 T allele is associated with high transcriptional activity of the promoter/enhancer region.[6] This might cause an enhanced mucosal release of TNF-α in response to *H. pylori* infection, and high mucosal levels of TNF-α has been suggested to play a pivotal role in the pathogenesis of duodenal ulcer.[7] *TNF-α* −308 SNP was correlated with *H. pylori* infection ($\chi^2 = 9.70$, $P < 0.05$), which was more frequent in *TNF-α* −308 A/G (61.2%) than in G/G (54.1%) subjects, in agreement with previous data by Yea et al.[8] in Korean patients. Antral inflammation was more severe in patients bearing *TNF α* −1031 T allele ($\chi^2 = 12.3$, $P < 0.05$) (Table 1). The presence or absence of intestinal metaplasia was not correlated with any of the studied cytokines' SNPs, but it was correlated with *H. pylori* antral density grade ($\chi^2 = 10.59$, $P < 0.05$) and with *cagA* (Fisher exact test, $P < 0.001$) or s1 *vacA* (Fisher exact test, $P < 0.001$). We suggest that *TNF-α* −308 and −1031 SNPs might be involved in favoring *H. pylori* infection and the inflammatory response of the infected gastric mucosa. *TNF-α* −857 T/T genotype might predispose to duodenal ulcer. *TNFα* SNPs in the promoter/enhancer region of the gene, do not seem involved in favoring the precancerous intestinal metaplasia or noncardia gastric cancer.

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Reply. We thank Zambon et al. for their interest in our paper and for sharing their data. Their study, comprising a heterogeneous group of upper gastrointestinal pathologies and including 129 gastric cancer cases, failed to find statistically significant associations between *IL-1B*-31 and *TNFA*-308 proinflammatory genotypes and gastric cancer or its precursors. However, their findings are at odds with a number of larger studies that have looked at these important markers. For example, there were 366 gastric cancer cases vs. 429 population controls in our earlier study based in Poland,[1] and this was confirmed in our U.S. study with 188 cases and 210 controls.[2] Machado et al. independently confirmed both *IL-1B*-511[3,4] and *TNFA*-308 findings in a study of 287 gastric cancer cases vs. 306 controls.[5] Furthermore, Rad et al.[6] and Furuta et al.[7] confirmed the association between *IL-1* markers and gastric premalignant abnormalities in Caucasian and Japanese populations, respectively.

We found it difficult to analyze or comment on the other findings in the study by Zambon et al. due to the lack of subject details and restriction of statistical data to χ^2 and P values. We also caution about their reported associations with the *TNFA* SNP's –1031 and -857 pending better definition of the functional significance of these genetic markers. Nevertheless, we agree with Zambon et al. about the important role of cytokine gene polymorphisms in the pathogenesis of *H. pylori*-related diseases.

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Discussion on Impaired Expression of Peroxisome Proliferator-Activated Receptor γ in Ulcerative Colitis

Dear Sir:

In their interesting paper on peroxisome proliferator-activated receptor (PPARγ) expression in inflammatory bowel disease (IBD), Dubuquoy et al.[1] examined colonic biopsies from patients with ulcerative colitis (UC), and Crohn's disease (CD). For control groups they used biopsies from patients with irritable bowel syndrome and sigmoid diverticulitis. We feel that clarification is required as to the true nature of the latter group in relation to its use as an inflammatory control.

Diverticulitis is a subserosal disease.[2] Narrow-necked diverticula can become obstructed by entrapped fecal matter. Hyperplasia of the mucosa-associated lymphoid tissue follows. Subsequent inflammation of the pericolic and mesenteric fat can lead to peridiverticular abscess formation. Mucosal inflammation, however, is not a prominent feature of diverticulitis.

In contrast, diverticular colitis is characterized by segmental mucosal inflammation, the proposed etiology of which is multifactorial.[3] Potential mechanisms include the mechanical action of firm stools on redundant mucosal folds leading to mucosal ischemia and prolonged exposure of the mucosa to luminal contents such as bacterial antigens and toxins. Endoscopically, mucosal hyperemia, granularity, edema, and ulceration can be identified on crescentic mucosal folds; diverticular orifices are usually spared.[4] The microscopic features include crypt abscesses and architectural distortion and are often indistinguishable from those found in idiopathic IBD.[5]

Since diverticular colitis is a predominantly mucosal disease, patients with this diagnosis would seem to be a more appropriate inflammatory control group than those with diverticulitis, which is primarily subserosal. An alternative and perhaps more readily accessible inflammatory control group would of course be patients with infective colitis.

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